Current Eye Research

ISSN: 0271-3683 (Print) 1460-2202 (Online) Journal homepage: www.tandfonline.com/journals/icey20

The Morpho-functional Evaluation of Retina in Amblyopia

Betul Tugcu, Bilge Araz-Ersan, Murat Kilic, Ezgi Tuna Erdogan, Ulviye Yigit & Sacit Karamursel

To cite this article: Betul Tugcu, Bilge Araz-Ersan, Murat Kilic, Ezgi Tuna Erdogan, Ulviye Yigit & Sacit Karamursel (2013) The Morpho-functional Evaluation of Retina in Amblyopia, Current Eye Research, 38:7, 802-809, DOI: 10.3109/02713683.2013.779721

To link to this article: https://doi.org/10.3109/02713683.2013.779721

Published online: 22 Mar 2013.

Current Eye Research, 2013; 38(7): 802–809
© Informa Healthcare USA, Inc.
ISSN: 0271-3683 print / 1460-2202 online
DOI: 10.3109/02713683.2013.779721

informa
healthcare

ORIGINAL ARTICLE

The Morpho-functional Evaluation of Retina in Amblyopia*

Betul Tugcu[1], Bilge Araz-Ersan[1], Murat Kilic[1], Ezgi Tuna Erdogan[2], Ulviye Yigit[1] and Sacit Karamursel[2]

[1]*Department of Ophthalmology, Bakirkoy Dr Sadi Konuk Education and Research Hospital, Istanbul, Turkey and* [2]*Department of Physiology, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkey*

ABSTRACT

Purpose: To investigate the morphological or functional differences of retina in amblyopia.

Materials and methods: Forty-one patients with unilateral strabismic, anisometropic or combined amblyopia were included in the study. A control group was composed of 16 normal children. All participants were tested with optical coherence tomography (OCT) and pattern electroretinography (PERG). The findings from amblyopic and nonamblyopic eyes were compared among the amblyopic groups. Also, amblyopic and nonamblyopic eyes were compared with the healthy control eyes.

Results: No significant difference was found in OCT parameters for amblyopic and nonamblyopic eyes among the amblyopic groups ($p > 0.05$). In the combined and anisometropic groups, ganglion cell complex (GCC) was found to be significantly increased in both amblyopic and nonamblyopic eyes compared to the control group ($p < 0.05$). In strabismic amblyopia, significant reduction in GCC thickness and increase in foveal thickness were found, compared to nonamblyopic eyes ($p = 0.019$, $p = 0.08$). There were no significant differences in PERG amplitude and latency between the amblyopic and the nonamblyopic eyes in amblyopic groups ($p > 0.05$). PERG amplitude in amblyopic eyes was found to be significantly decreased compared with that in normal eyes ($p < 0.05$). When the nonamblyopic eyes were compared with the control group, only the anisometropic amblyopia group demonstrated significant reduction in amplitude and prolongation in latency ($p = 0.002$, $p = 0.026$).

Conclusion: We found no significant differences in morphological and functional measures among amblyopic groups. However, we detected significant differences in the retinal function and morphology of both amblyopic and nonamblyopic eyes compared with healthy control eyes.

Keywords: Amblyopia, optical coherence tomography, pattern electroretinogram

INTRODUCTION

Amblyopia is a disorder of the visual system that is characterized by reduction in best corrected visual acuity (VA). It is unilateral, or less commonly bilateral, and caused by abnormal visual experience early in life resulting from visual deprivation, strabismus, anisometropia or high bilateral refractive errors.[1] The neural sites that are involved in amblyopia are still under investigation. Although the loss of VA is considered to be cortical in origin, abnormalities of retinal ganglion cells (RGC) were reported in animal studies.[2–4] Moreover, abnormal RGC function, determined by pattern electroretinography (PERG),[5–8] and structural retina changes, detected by optical coherence tomography (OCT), were also observed in humans.[9–12]

Retinal structure and function in amblyopia is a topic of broad interest, and previous studies on this subject have produced inconclusive and controversial

*This paper was presented in the XIth Meeting of the International Strabismological Association 2010, Istanbul, Turkey.

Received 18 May 2012; revised 7 February 2013; accepted 20 February 2013; published online 21 March 2013

Correspondence: Dr Betul Tugcu, Department of Ophthalmology, Bakirkoy Dr Sadi Konuk Education and Research Hospital, Tevfik Saglam Street, No:11 Zuhuratbaba, Istanbul 34147, Turkey. Tel: 90 (532) 446 06 81. Fax: +90 (212) 542 44 91. E-mail: betultugcu@yahoo.com

results.[5–22] Racial differences, measurement error among examiners, low sample sizes, the grouping of various types of amblyopia together, the use of different versions of the OCT scanning algorithms and differences in subjects' ages have been suggested as potential confounding factors.[16] In this study, by taking advantage of two approaches, OCT and PERG, we aimed to identify the existence of any structural or functional abnormalities of the retina in amblyopic and nonamblyopic eyes among the amblyopic subgroups. Furthermore, we compared amblyopic and nonamblyopic eyes with the healthy control eyes in order to evaluate retinal involvement in amblyopia.

MATERIALS AND METHODS

Forty-one patients with unilateral amblyopia were included in this study. The patients were all Caucasians, and divided into three groups according to the cause of amblyopia. The causes of amblyopia were strabismus ($n=14$), anisometropia ($n=14$) and combined anisometropia and strabismus ($n=13$). Sixteen normal children served as controls. Approval for this study was obtained from the institutional review board of Bakirkoy Education and Research Hospital. The study was performed according to the tenets of the Declaration of Helsinki for research involving human subjects. Written informed consent was obtained from the parents of the participating patients.

Patients with histories of preterm birth, severe amblyopia, neurological diseases or ocular diseases such as glaucoma or nystagmus, as well as patients who were too young to cooperate (<7 years), were excluded from this study. One eye of each healthy volunteer was selected randomly to compose the age-matched control group. All patients and healthy volunteers underwent a complete ophthalmic and orthoptic examination. Best corrected VA was measured with a Snellen chart at 6 m. VA readings were transformed to a logarithmic scale (logMAR) for statistical analysis. Fixation behavior was evaluated by having the patient fixate on an accommodative target held at 40 cm with best correction in place. Only patients with central, steady and maintained fixation were included in the study. PERG and OCT examination were performed by the same examiner for all participants.

Unilateral amblyopia was defined as a difference of at least two lines on the acuity chart between the amblyopic and the nonamblyopic eyes. The VA of the nonamblyopic eye of the study group was 0.00 logMAR, and there was no amblyogenic risk factor. Unilateral amblyopia was defined as a difference of at least 0.1 logMAR between the two eyes. Anisometropia was diagnosed in those patients whose spherical equivalance showed 1.5 diopters (D) or greater difference between the two eyes in hyperopia, and 3 D or greater difference in myopia. Patients having constant and nonalternating strabismus were classified as strabismic ambliyopia. Patients with anisometropia and strabismus were classified as combined amblyopia. Amblyopia was classified as mild, moderate or severe, based on whether VA in the amblyopic eye was 0.5–0.9, 0.2–0.5 or <0.2, respectively.

The children with amblyopia included 19 males and 22 females, and their mean age was 12.31 ± 3.28 years (age range: 7–14 years). The control group used in this study included nine males and seven females, and their mean age was 10.63 ± 1.74 (age range: 7–15 years). There were no significant differences in the mean age values of the amblyopic groups and control group ($p=0.154$).

OCT images were obtained using the Optovue RTVue Fourier domain OCT (RTVue-100, 2007, version 5.1, Optovue Inc., Fremont, CA). OCT was performed without pupil dilation. In order to reduce the effect of refractive error on OCT testing, all eyes with a refractive spherical equivalant (myopic or hyperopic) >5 D or with astigmatism >3 D were excluded from this study. Furthermore, our patients were selected on the basis of their ability to maintain steady fixation on the OCT, and each scan was accurately checked to avoid misaligment of foveal imaging. Each OCT scan was performed by the same examiner. An internal fixation target was used, and the patient's fellow eye was covered during scanning. Each eye underwent NHM4, MM5 and ganglion cell complex (GCC) scan protocols. MM5 scan protocol measures the macular retinal thickness map with a $5 \times 5\,mm^2$ grid centered on fixation. The map of macular thickness was composed of three concentric circles: a central circle (fovea), an inner ring (parafovea) and an outer ring (perifovea). Macular volume (MV) within 1, 3 and 5 mm was measured. NHM4 scans measure RNFL thickness and the optic disc. The GCC scan protocol measures the GCC layer, which encompasses the RNFL, ganglion cell bodies and inner plexiform layer. It has one horizontal line of 7 mm in scan length, followed by 15 vertical lines of 6 mm scan lengths and 0.5 mm intervals, centered 1 mm temporal to the fovea.

The PERG was recorded according to the ISCEV (International Society for Clinical Electrophysiology of Vision) standards. A Nihon Kohden polygraph system (Nihon Kohden, Tokyo, Japan) and silver cup electrodes were used for recordings. The active electrode was placed over the nasal canthus, and the reference electrode was placed on the ipsilateral temple, 2 cm from the eyeball, while the ground electrode was placed on the contralateral ear lobe. Subjects were seated 1 m from the monitor and signals were recorded while they looked at a fixation point with the other eye occluded. Refractive errors of all subjects were corrected during recording. The

TABLE 1 Comparison of the mean GCC and foveal thickness, macular volume, total RNFL in amblyopic and nonamblyopic eyes among amblyopic groups.

		Strabismic	Anisometropic	Combined	F	p
Amblyopic	GCC (μm)	99.29 ± 9.56	104.25 ± 6.25	104.15 ± 6.53	1.95	0.156
	Foveal thickness (μm)	276.36 ± 25.54	277.36 ± 43.13	265.43 ± 30.21	0.54	0.589
	Macular volume (mm^3)	6.18 ± 0.36	5.81 ± 1.69	6.05 ± 0.29	0.47	0.627
	Total RNFL (μm)	115.27 ± 13.71	112.93 ± 14.74	116.13 ± 10.39	0.22	0.800
Nonamblyopic	GCC (μm)	103.08 ± 7.55	105.27 ± 6.14	104.36 ± 6.76	0.36	0.698
	Foveal thickness (μm)	258.43 ± 23.99	263.14 ± 22.28	260.29 ± 22.17	0.15	0.860
	Macular volume (mm^3)	6.07 ± 0.33	6.16 ± 0.22	6.07 ± 0.29	0.48	0.620
	Total RNFL (μm)	115.65 ± 16.01	118.83 ± 11.15	116.60 ± 12.54	0.21	0.814

stimulus was an alternating white and black checkerboard pattern (100 stimuli), and stimulus reversal was 2 Hz. The analog filter was arranged between 0.01 and 100 Hz for PERG. Electrode impedences were kept below 5 kOhm. The data was analysed in the Physiology Department of İstanbul Medical Faculty with Electrophysiological Recording and Analysis System Programme. The data were filtered between 1 and 30 Hz before analysis. Manual artifact rejection was applied to data for eye movement artifacts. P50-N95 amplitude peak to peak and latencies of P50 and N95 were measured.

Statistical analyses were performed using NCSS (Number Cruncher Statistical System 2007, Kaysville, UT). The significance level was set at a p value of less than 0.05. Statistical analysis for the comparison of OCT and PERG parameters among the amblyopic groups and control group was performed using the ANOVA test. An unpaired t-test was used to compare the OCT and PERG parameters of the amblyopic, nonamblyopic and healthy control eyes. Bonferonni correction was used to control for false positives. The correlation between OCT and PERG parameters was determined using Pearson's correlation coefficient.

RESULTS

The mean VA (logMAR) was 0.32 ± 0.2 in the combined amblyopia group, 0.3 ± 0.17 in the anisometropic group, and 0.19 ± 0.09 in the strabismic group ($p = 0.11$). There was no significant difference in the depth of amblyopia of the amblyopic eyes among the amblyopic groups ($p = 0.21$).

Hyperopia was noted in 11 cases and myopia was noted in three cases in the anisometropic amblyopia group. Among patients with strabismus, esotropia was noted in 12 cases and exotropia was noted in two cases. In all amblyopic cases, hyperopia was noted in 37 (91%) cases and myopia in four (9%) cases. The mean hyperopic refractive errors of amblyopic eyes and nonamblyopic eyes were 3.80 ± 2.17 and 2.74 ± 2.15 D, respectively, ($p = 0.0001$). The mean myopic refractive errors of amblyopic eyes and nonamblyopic eyes were 1.93 ± 3.19 and 0.8 ± 1.33 D, respectively, ($p = 0.544$).

In a comparison of OCT parameters regarding total RNFL, GCC, foveal thickness and macular volume, no significant difference was found between amblyopic and nonamblyopic eyes among the amblyopic groups ($p > 0.05$) (Table 1, ANOVA test). When OCT parameters were compared among amblyopic, nonamblyopic and control eyes in the combined and anisometropic groups, GCC was found to be significantly increased in both amblyopic and nonamblyopic eyes compared to the control group ($p > 0.05$). Only in the children with strabismic amblyopia, significant reduction in GCC thickness and increase in foveal thickness were found in amblyopic eyes compared to nonamblyopic eyes ($p = 0.019$, $p = 0.08$; Table 2, unpaired t-test).

Based on known retinal topography, axons of RGCs recruited by PERG stimulus are expected to enter the disc in the temporal sector.[23] For this reason, the peripapillary RNFL thickness measurements were also assessed for the temporal, inferior, nasal and superior quadrants. In comparison of the mean RNFL thickness in four quadrants, there were no significant differences in the amblyopic and nonamblyopic eyes among amblyopic groups and the control group ($p > 0.05$; Table 3, ANOVA test). When subgroups were compared, while the temporal RNFL of the strabismic amblyopic eyes were thinner than the nonamblyopic eyes, in the anisometropic amblyopia group, the inferior RNFL of the amblyopic eyes were found to be thinner than nonamblyopic eyes and healthy control eyes (respectively: $p = 0.026$, $p = 0.036$, $p = 0.034$; Table 4, unpaired t-test).

An analysis of PERG parameters found no significant differences in PERG amplitude and latency between the amblyopic and the non-amblyopic eyes in the three amblyopic groups ($p > 0.05$). When the amblyopic eyes of three amblyopic groups were compared with the healty control eyes, the mean PERG amplitude was found to be significantly decreased ($p < 0.05$). Furthermore, when the nonamblyopic eyes of amblyopic groups were compared, reduction in amplitude and prolongation in latency

TABLE 2 Comparison of GCC, foveal thickness, macular volume and total RNFL among amblyopic, nonamblyopic and normal control eyes in amblyopic groups.

					Amb/control		Nonamb/control		Amb/nonamb	
		Amblyopic	Nonamblyopic	Control	t	p	t	p	t	p
Strabismic	GCC (μm)	99.29 ± 9.56	103.08 ± 7.55	99.55 ± 5.44	−0.11	0.913	1.67	0.104	−2.67	0.019
	Foveal thickness (μm)	276.36 ± 25.54	258.43 ± 23.99	265.46 ± 20.02	1.46	0.153	−0.97	0.338	3.12	0.008
	Macular volume (mm^3)	6.18 ± 0.36	6.07 ± 0.33	6.07 ± 0.35	0.91	0.368	0.05	0.960	1.72	0.108
	Total RNFL (μm)	115.27 ± 13.71	115.65 ± 16.01	114.80 ± 9.84	0.12	0.903	0.12	0.903	−0.18	0.857
Anisometropic	GCC (μm)	104.25 ± 6.25	105.27 ± 6.14	99.55 ± 5.44	2.43	0.02	2.98	0.005	−1.23	0.24
	Foveal thickness (μm)	277.36 ± 43.13	263.14 ± 22.28	265.46 ± 20.02	1.16	0.253	−0.33	0.743	1.42	0.18
	Macular volume (mm^3)	5.81 ± 1.69	6.16 ± 0.22	6.07 ± 0.35	−0.73	0.472	0.92	0.363	−0.79	0.446
	Total RNFL (μm)	112.93 ± 14.74	118.83 ± 11.15	114.80 ± 9.84	−0.47	0.641	−0.47	0.641	−1.87	0.084
Combined	GCC (μm)	104.15 ± 6.53	104.36 ± 6.76	99.55 ± 5.44	2.33	0.025	2.40	0.022	−0.30	0.77
	Foveal thickness (μm)	265.43 ± 30.21	260.29 ± 22.17	265.46 ± 20.02	−0.01	0.997	−0.74	0.465	1.11	0.287
	Macular volume (mm^3)	6.05 ± 0.29	6.07 ± 0.29	6.07 ± 0.35	−0.19	0.854	0.04	0.965	−0.99	0.34
	Total RNFL (μm)	116.13 ± 10.39	116.60 ± 12.54	114.80 ± 9.84	0.39	0.696	0.39	0.696	−0.26	0.796

TABLE 3 Comparison of the mean RNFL thickness in four quadrants of amblyopic and nonamblyopic eyes among amblyopic groups.

		Strabismic	Anisometropic	Combined	F	p
Amblyopic	Temp RNFL (μm)	78.5 ± 17.81	82.89 ± 7.74	82.95 ± 14.89	0.44	0.645
	Sup RNFL (μm)	133.35 ± 21.47	137.38 ± 28.77	135.47 ± 20.32	0.10	0.907
	Nasal RNFL (μm)	94.86 ± 18.01	90.35 ± 20.65	92.99 ± 14.19	0.22	0.804
	Inf RNFL	154.05 ± 30.43	142.32 ± 20.25	148.78 ± 24.37	0.72	0.495
Nonamblyopic	Temp RNFL (μm)	90.44 ± 20.29	88.09 ± 14.05	84.1 ± 15.34	0.51	0.607
	Sup RNFL (μm)	136.9 ± 22.61	141.42 ± 17.66	132.74 ± 14.42	0.74	0.485
	Nasal RNFL (μm)	87.84 ± 23.38	97.36 ± 39.76	91.63 ± 19.54	0.38	0.688
	Inf RNFL (μm)	154.18 ± 33.67	149.56 ± 22.7	157.95 ± 30.3	0.28	0.761

TABLE 4 Comparison of the RNFL thickness in four quadrants among the amblyopic, nonamblyopic and normal control eyes in amblyopic groups.

					Amb/control		Nonamb/control		Amb/nonamb	
		Amblyopic	Nonamblyopic	Control	t	p	t	p	t	p
Strabismic	Temporal RNFL (μm)	78.5 ± 17.81	90.44 ± 20.29	83.60 ± 16.20	−0.90	0.372	1.14	0.261	−2.50	0.026
	Nasal RNFL (μm)	94.86 ± 18.01	87.84 ± 23.38	84.36 ± 17.03	1.79	0.081	0.53	0.601	0.93	0.370
	Inferior RNFL (μm)	154.05 ± 30.43	154.18 ± 3367	156.68 ± 18.54	−0.33	0.742	−0.30	0.769	−0.02	0.983
	Superior RNFL (μm)	133.35 ± 21.47	136.9 ± 22.61	132.50 ± 19.01	0.13	0.900	0.64	0.526	−0.74	0.472
Anisometropic	Temporal RNFL (μm)	82.89 ± 7.74	88.09 ± 14.05	83.60 ± 16.20	−0.15	0.882	0.84	0.407	−0.90	0.384
	Nasal RNFL (μm)	90.35 ± 20.65	97.36 ± 39.76	84.36 ± 17.03	0.95	0.350	1.39	0.172	−0.52	0.613
	Inferior RNFL (μm)	142.32 ± 20.25	149.56 ± 22.7	156.68 ± 18.54	−2.18	0.036	−1.03	0.310	−2.40	0.034
	Superior RNFL (μm)	137.38 ± 28.77	141.42 ± 17.66	132.50 ± 19.01	0.62	0.539	1.39	0.172	−0.57	0.580
Combined	Temporal RNFL (μm)	82.95 ± 14.89	84.1 ± 15.34	83.60 ± 16.20	−0.12	0.902	0.09	0.926	−0.23	0.823
	Nasal RNFL (μm)	92.99 ± 14.19	91.63 ± 19.54	84.36 ± 17.03	1.60	0.119	1.20	0.237	0.20	0.847
	Inferior RNFL (μm)	148.78 ± 24.37	157.95 ± 30.3	156.68 ± 18.54	−1.13	0.267	0.16	0.873	−1.41	0.183
	Superior RNFL (μm)	135.47 ± 20.32	132.74 ± 14.42	132.50 ± 19.01	0.45	0.654	0.04	0.969	0.44	0.665

was found only in the anisometropic amblyopia group (respectively: $p = 0.002$, $p = 0.026$; Tables 5 and 6, ANOVA test).

In all patients, we also assessed PERG amplitude and latency of the amblyopic eyes in comparison with the nonamblyopic eyes and control eyes (Figure 1). The differences between eyes were statistically significant in amplitude and latency ($p < 0.05$). These differences were derived from significant differences in mean PERG amplitude and latency between amblyopic and healthy control eyes ($p = 0.001$ and $p = 0.022$, respectively). Significant differences in PERG amplitude were also found between nonamblyopic eyes and healthy control eyes ($p = 0.01$).

TABLE 5 Comparison of the mean PERG amplitude of the amblyopic and nonamblyopic eyes among amblyopic groups and normal eyes of control group.

	Strabismic	Anisometropic	Combined	Control	F	p
Amb PERG amp (μV)	1.86 ± 1.58	1.58 ± 1.73	1.89 ± 1.07	2.63 ± 1.78	4.65	0.005
Nonamb PERGamp (μV)	2.05 ± 0.70	1.63 ± 0.50	2.07 ± 0.99	2.63 ± 1.78	3.86	0.014

Tukey multiple comparison test		Amb PERG p	Nonamb PERG p
	Strabismic versus anisometropic	0.679	0.356
	Strabismic versus combined	0.534	0.782
	Strabismic versus control	0.034	0.141
	Anisometropic versus combined	0.329	0.046
	Anisometropic versus control	0.003	0.002
	Combined versus control	0.01	0.074

TABLE 6 Comparison of the mean PERG latency of the amblyopic and nonamblyopic eyes among amblyopic groups and normal eyes of control group.

	Strabismic	Anisometropic	Combined	Control	F	p
Amb PERG latency (ms)	52 ± 7.46	51 ± 5.42	52.93 ± 8.97	47.5 ± 5.93	2.29	0.086
Nonamb PERG latency (ms)	51 ± 5.43	53.15 ± 5.56	47.86 ± 5.47	47.5 ± 5.93	3.52	0.02

Tukey multiple comparison test		Nonamb PERG p
	Combined versus anisometropic	0.082
	Combined versusstrabismic	0.462
	Combined versus control	0.998
	Anisometropic versus strabismic	0.757
	Anisometropic versus control	0.026
	Strabismic versuscontrol	0.266

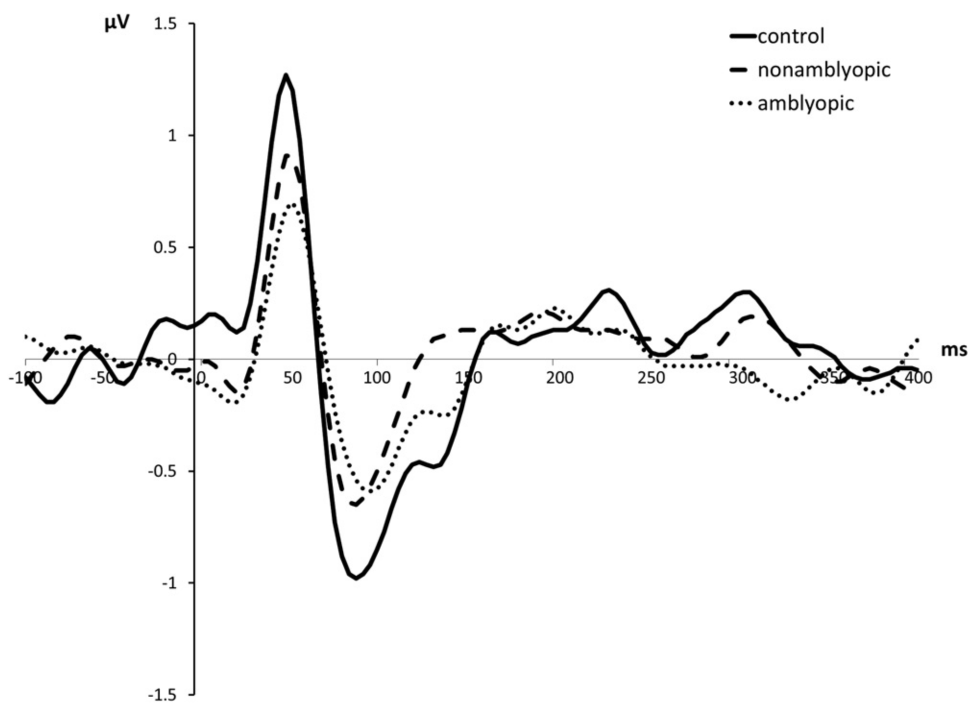

FIGURE 1 PERG Grand average of amblyopic, non-amblyopic and control normal eyes in all subjects.

However, no significant difference in PERG latency was found between nonamblyopic eyes and healthy control eyes ($p = 0.138$).

No statistically significant correlations were found between OCT and PERG parameters ($r = -0.041$, $r = -0.043$, $r = -0.055$, $r = 0.235$, $p > 0.05$). There was no correlation between VA and OCT or PERG parameters ($r = -0.034$, $r = -0.003$, $r = 0.014$, $r = -0.047$, $r = 0.005$, $r = -0.05$, $p > 0.05$). The correlations between hyperopic refractive error and OCT and PERG parameters were also not significant ($r = -0.246$, $r = 0.000$, $r = -0.317$, $r = 0.098$, $r = 0.205$, $r = 0.091$, $p > 0.05$).

DISCUSSION

In our study, we found no significant differences in OCT and PERG parameters among amblyopic groups; however, in the strabismic amblyopic eyes, significant increases in foveal thickness, and reductions in temporal RNFL and GCC layer thicknesses compared to nonamblyopic eyes were found. In addition, in the combined and anisometropic groups, GCC in both amblyopic and nonamblyopic eyes was found to be significantly increased compared to the healthy control eyes. Although these differences were small, they exceeded the variability of the repeatability and reproducibility of FD-OCT owing to higher speed and resolution.[24]

In spite of the fact that the basic mechanisms in different types of amblyopia are similar, certain clinical differences exist between strabismic and anisometropic amblyopia in terms of severity, psychophysical characteristics and reversibility.[25] The differences in thicknesses of the fovea, GCC and RNFL according to the type of amblyopia have been thought to be due to these differences in the neurophysiological mechanisms between anisometropic and strabismic amblyopia.[26] Moreover, thickening of the amblyopic fovea has been attributed to a developmental arrest, with incomplete formation of the foveal depression.[27] Finally, further research has been suggested to determine whether these structural abnormalities are due to an expression disorder of the retina development gene.[28]

PERG obtains unique information on the reduced responsiveness of viable RGCs. Conflicting results have been reported as to whether the amplitude of PERG is reduced in amblyopia. Several authors have described a large reduction of the PERG amplitude in amblyopia studies.[5–8] In our study, also, significant reduction of the PERG amplitudes of amblyopic eyes of amblyopic groups was found, compared to the control group. We thought that this difference was significant owing to the lack of variability of repeatability and reproducibility of PERG. Since the pERG data is the average of responses to 100 stimuli and was 1–30 Hz band-pass filtered before the P50 & N95 peak measurements, the repeatability of the measurement is not questionable. However, other authors argued that when fixation alignment and stability were individually optimized in amblyopic eyes with low VA, PERG deficit was not observed. In these studies, the patients' ages ranged from 9 to 60 years, whereas the ages of the control group ranged from 18 to 34 years.[13,14] On the contrary, our study was conducted with more homogenous groups and similar ranges (7–14 years) of ages, and the patients had good foveal fixation.

In unilateral amblyopia, VA is often considered to be normal in the fellow eye; however, subtle deficits in other visual functions have been reported. In the present study, when the nonamblyopic eyes were compared with the healthy control eyes, only the anisometropic amblyopia group demonstrated significant reduction in PERG amplitude and prolongation in latency. It has been reported that in anisometropic amblyopia, the functional imbalance between the two eyes may lead to permenant changes that affect not only the visual pathway associated with the amblyopic eye but also the pathway associated with the fellow eye.[29] Also, in anisometropic amblyopia, reduction of the PERG amplitude of the fellow eye due to occlusion in younger children has been reported in the a previous study.[5]

The significant relationships between the structure and function of amblyopia are important because they can provide information on the extent of neural substrate and its effect on visual function.[24] In the literature, the relationship between RNFL and visual sensitivity has been investigated to determine the degree to which anatomic measurements reflect visual sensitivity.[30,31] A similar study evaluating the structure and function of retina in amblyopia was performed using OCT and microperimetry. It was found that strabismic amblyopes had thicker fovea, and macular sensitivity was reduced in both strabismic and anisometropic amblyopes. RNFL thickness and macular sensitivity were found to be significantly correlated.[24] Likewise, foveal thickness was increased in amblyopic eyes compared to nonamblyopic eyes in strabismic amblyopia, and mean PERG amplitudes of amblyopic eyes were decreased compared to healthy control eyes in the present study. However, no significant correlations were found between OCT and PERG parameters.

Although this is a comprehensive study evaluating both retinal structure and function, we are aware that our study is limited by the small sample size owing to the rigorous patient selection protocol. During the enrollment phase of the study, many patients were excluded, in order to constitute more homogenous groups without significant differences in age, depth of amblyopia, VA and refraction. Furthermore, in order to reduce the effect of refractive error on OCT testing, all eyes with a refractive error of spherical equivalant >5 D or with astigmatism >3 D were excluded. In addition, our patients were selected on the basis of their ability to maintain central steady fixation on the OCT, and each scan was accurately checked to avoid misaligment of foveal imaging. For this purpose, severe amblyopes were also excluded from the study.

In conclusion, statistically significant differences in PERG parameters between amblyopic and healthy control eyes and a lack of correlation between OCT and PERG parameters support functional visual loss in amblyopia. No significant difference was found in morphological and functional measures among the amblyopic groups. However, we detected significant differences in the retinal function and morphology of both amblyopic and nonamblyopic eyes compared with healthy control eyes. Further studies with larger groups are warrented to confirm the results of the present study.

ACKNOWLEDGEMENTS

The authors thank Dr Rana Konyalioglu for the statistical analysis.

Ethics approval was provided by the Institutional Review Board of Bakirkoy Education and Research Hospital and this study conformed to the requirements of the principles of the Declaration of Helsinki. Informed consent was obtained from the parents of all patients.

DECLARATION OF INTEREST

The authors have no conflict of interest with the submission. No financial support was received for this submission.

REFERENCES

1. Day S. Normal and abnormal visual development. In: Taylor D, editor. Pediatric ophthalmology. 1st ed. Vol. 1, chapter 2. London: Blackwell Scientific Publications; 1990 pp 7–20.
2. Ikeda H, Tremain KE. Amblyopia occurs in retinal ganglion cells in cats reared with convergent squint without alternating fixation. Exp Brain Res 1979;35:559–582.
3. Chino YM, Sansky MS, Hamasaki DI. Developmant of receptive field properties of retinal ganglion cells in kittens raised with a convergent squint. Exp Brain Res 1980;39: 313–320.
4. Sosula L, Glow PH. Increase in number of synapses in the inner plexiform layer of the light deprived rat retinae:quantitative electron microscopy. J Comp Neurol 1971;141:427–451.
5. Arden GB, Wooding SL. Pattern ERG in Amblyopia. Invest Ophthalmol Vis Sci 1985;26:88–96.
6. Sokol S, Nadler D. Simultaneous electroretinograms and visual evoked potentials from adult amblyopies in response to pattern stimuli. Invest Ophthalmol Vis Sci 1979;18:848–855.
7. Arden GB, Vaegan, Hogg CG, Powell DJ, Carter RM. attern ERG s are abnormal in many amblyopes. Trans Ophthalmol Soc UK 1980;100:453–460.
8. Wanger P, Person HE. Oscillatory potentials, flash and pattern reversal electroretinograms in amblyopia. Acta Ophthalmol 1984;62:643–650.
9. Yoon SW, Park WH, Baek SH, Kong SM. Thickness of macular retinal layer and peripapillary retinal nerve fiber layer in patients with hyperopic anisometropic amblyopia. Korean J Ophthalmol 2005;19:62–67.
10. Yen MY, Cheng CY, Wang AG. Retinal nerve fiber layer thickness in unilateral amblyopia. Invest Ophthalmol Vis Sci 2004;45:2224–2230.
11. Al-Haddad CE, Mollayess GM, Cherfan CG, Jaafar DF, Bashshur ZF. Retinal nerve fibre layer and macular thickness in amblyopia as measured by spectral-domain optical coherence tomography. Br J Ophthalmol 2011;95: 1696–1699.
12. Aguirre F, Mengual E, Hueso JR, Moya M. Comparison of normal and amblyopic retinas by optical coherence tomography in children. Eur J Ophthalmol 2010;20: 410–418.
13. Hess RF, Baker CL, Verhoeve JN, Keesey UT, D France T. The pattern evoked electroretinogram: ıts variability in normals and its relationship to amblyopia. Invest Ophthalmol Vis Sci 1985;26:1610–1623.
14. Gottlob I, Welge Lüssent L. Normal pattern electroretinograms in amblyopia. Invest Ophthalmol Vis Sci 1987;28: 187–191.
15. Repka MX, Kraker RT, Tamkins SM, Suh DW, Sala NA, Beck RW; for Pediatric Eye Disease Investigator Group. Retinal nerve fiber layer thickness in amblyopic eyes. m J Ophtalmol 2009;148:143–147.
16. Kee SY, Lee SY, Lee YC. Thickness of the fovea and retinal nerve fiber layer in amblyopic and normal eyes in children. Korean J Ophthalmal 2006;20:177–181.
17. Atilla H, Batioğlu F, Erkam N. Retinal nerve fiber analysis in subject with hyperopia and anisometropic amblyopia. Binocul vis Strabismus Q. 2005;20:33–37.
18. Altintas O, Yüksel N, Ozkan B, Cağlar Y. Thickness of the retinal nerve fiber layer, macular thickness and macular volume in patients with strabismic amblyopia. J Pediatr Ophthalmol Strabismus 2005;42:216–221.
19. Park KA, Park do Y, Oh SY. Analysis of spectral-domain optical coherence tomography measurements in amblyopia: a pilot study. Br J Ophthalmol 2011;95:1700–1706.
20. Bozkurt B, Irkec M, Orhan M, Karaagaoğlu E. Thickness of the retinal nerve fiber layer in patients with anisometropic and strabismic amblyopia. Strabismus 2003;11:1–7.
21. Baddini-Caramelli C, Hatanaka M, Polati M, Umino AT, Susanna Jr R. Thickness of the retinal nerve fiber layer in amblyopic and normal eyes; a scanning laser polarimetry study. JAAPOS 2001;5:82–84.
22. Dickmann A, Petroni S, Perrotta V, Salerni A, Parrilla R, Aliberti S, et al. A morpho-functional study of amblyopic eyes with the use of optical coherence tomography and microperimetry. JAAPOS 2011;15:338–341.
23. Ventura LM, Sorokac N, De Los Santos R, Feuer WJ, Porciatti V. The relationship between retinal ganglion cell function and retinal nerve fiber thickness in early glaucoma. Invest Ophthalmol Vis Sci 2006;47:3904–3911.
24. Bruce A, Pacey IE, Dharni P, Scally AJ, Barrett BT. Repeatability and reproducibility of macular thickness measurements using fourier domain optical coherence tomography. Open Ophthalmol J 2009;3:10–14.
25. Von Noorden GK. Mechanism of amblyopia. Doc Ophthalmol 1977;34:93–115.
26. Choi MY, Lee KM, Hwang JM, Choi DG, Lee DS, Park KH, Yu SY. Comparison between anisometropic and strabismic amblyopia using functional magnetic resonance imaging. Br J Ophthalmol 2001;85:1052–1056.
27. Provis JM, Diaz CM, Penfold PL. Microglia in human retina:a heterogeneous population wit distinct ontogenesis. Perspect Dev Neurobiol 1996;3:213–221.
28. Liu H, Zhong L, Zhou X, Jin QZ. Macular abnormality observed by optical coherence tomography in children with amblyopia failing to achieve normal visual acuity after long-term treatment. J Pediatr Ophthalmol Strabismus 2010;47:17–23.

29. Huang CB, Zhou J, Lu ZL, Zhou Y. Deficient binocular combination reveals mechanisms of anisometropic amblyopia: signal attenuation and interocular inhibition. J Vis 2011;11:1–17.
30. Kanamori A, Naka M, Nagai-Kusuhara A, Yamada Y, Nakamura M, Negi A. Regional relationship between retinal nerve fiber layer thickness and corresponding visual field sensitivity in glaucomatous eyes. Arch Ophthalmol 2008;126:1500–1506.
31. Horn FK, Mardin CY, Laemmer R, Baleanu D, Juenemann AM, Kruse FE, Tornow RP. Correlation between local glaucomatous visual field defects and loss of nerve fiber layer thickness measured with polarimetry and spectral domain OCT. Invest Ophthalmol Vis Sci 2009;50:1971–1977.